

8. (Amended) Nuclei of vertebrate cells comprising a modified genome obtainable by the method of claim 1.

10. (Amended) A method for generation of transgenic vertebrates characterized by injecting regenerative vertebrate cells according to claim 7 into blastocysts of said vertebrate.

### REMARKS

The claim amendments eliminate multiple dependent and multiple/multiple dependent claims, but otherwise leave the substance of the claims unchanged. Early favorable consideration is respectfully requested.

Respectfully submitted,

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Attachment

**VERSION WITH MARKINGS TO SHOW CHANGES MADE****In The Claims**

1. (Amended) A method for repetitive DNA expression cassette exchange in the genome of cells or parts of cells comprising the steps of

- a) integrating into a chromosomal locus of the genome of said cells a first DNA expression cassette carrying a positive-negative selection marker flanked by a wild type FLP-recombinase recognition target (FRT) site on one end and a modified heterospecific FRT site on the other end for tagging,
- b) selecting cell clones surviving the conditions for positive selection,
- c) exchanging said first DNA expression cassette against an incoming second DNA expression cassette located on a circular vector and carrying a homologous or heterologous gene (transgene) of any coding sequence flanked by the same FRT sites as said first DNA expression cassette mediated by the action of FLP-recombinase,

~~[characterized in that] wherein said cells are vertebrate cells which can regenerate to complete organisms, and said parts of cells are nuclei of vertebrate cells, which can be inserted into regenerative cells, and [further characterized by] wherein~~

- d) maintaining the conditions for positive selection during cultivation of said cells obtained in step b) while exchanging said first DNA expression cassette against said incoming second DNA expression cassette.
- e) using in step c) an incoming second DNA expression cassette which is marker-free, and
- f) selecting cell clones obtained after step c) surviving the conditions for negative selection.

3. (Amended) The method according to claim 1 [or 2] wherein said modified heterospecific FRT site is a FRT spacer mutant.

5. (Amended) The method [according to any of the preceding claims] of claim 1 wherein said [regenerative] vertebrate cells which can be regenerated are vertebrate embryonic stem (ES) cells.

7. (Amended) Regenerative vertebrate cells comprising a modified genome obtainable by [a method according to any one of claims 1 to 6] the method of claim 1.

8. (Amended) Nuclei of vertebrate cells comprising a modified genome obtainable by [a method according to any one of claims 1 to 6] the method of claim 1.

10. (Amended) A method for generation of transgenic vertebrates characterized by injecting regenerative vertebrate cells according to claim 7 [or 9] into blastocysts of said vertebrate.